

--This application is a divisional of U.S. Serial No. 09/695,807, filed October 23, 2000, now pending, which is a continuation-in-part of U.S. Serial No. 09/421,545, filed 20 October 1999, now pending, which is a continuation-in-part of U.S. Serial No. 09/361,775, filed 27 July 1999, now pending, which is a continuation-in-part of U.S. Serial No. 09/113,947, filed 10 July 1998, now pending. The contents of these applications are incorporated herein by reference.--

**IN THE CLAIMS:**

Please cancel claims 1-24, 26 and 28-44 without any prejudice and disclaimer.

Please replace claim 25 with the following clean set of amended claim 25. A mark-up version of the amended claim 25 is attached hereto as Exhibit A.

*Sub C1*  
25. (Amended) A method to treat a mammalian subject for a condition benefited by stimulating hair growth which method comprises administering to said mammalian subject in need of such treatment an effective amount of a compound that inhibits proteasomal activity or that inhibits production of proteasome proteins.

Please add new claims 45-70 as follows:

*Sub C1*  
45. (New) The method of claim 25, wherein the compound inhibits the chymotrypsin-like activity of the proteasome.

46. (New) The method of claim 45, wherein the compound is a peptide having at least 3 amino acids and a C-terminal functional group that reacts with the threonine residue of the chymotrypsin-like catalytic site of the proteasome.

*but C1*

47. (New) The method of claim 46, wherein the C-terminal functional group is selected from the group consisting of an epoxide, a -B(OR)<sub>2</sub> group, a -S(OR)<sub>2</sub> group and a -SOOR group, wherein R is H, an alkyl (C<sub>1-6</sub>) or an aryl (C<sub>1-6</sub>).

*Q3*

48. (New) The method of claim 47, wherein the functional group is an epoxide that forms a morpholino ring with the threonine residue of the chymotrypsin-like catalytic site of the proteasome.

*cont*

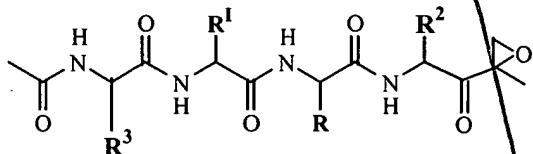
49. (New) The method of claim 45, wherein the peptide is a peptide  $\alpha'$ ,  $\beta'$ -epoxyketone.

50. (New) The method of claim 49, wherein the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone has at least 4 amino acids.

51. (New) The method of claim 49, wherein the c-terminus amino acid of the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone is a hydrophobic amino acid.

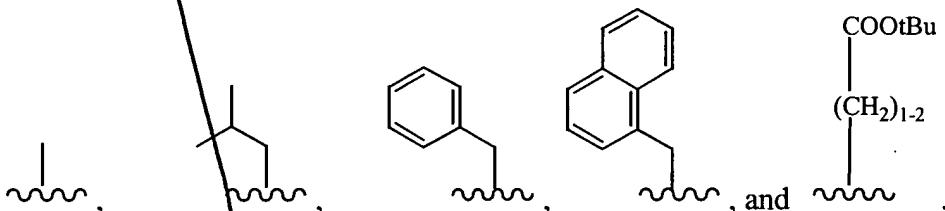
52. (New) The method of claim 51, wherein the hydrophobic amino acid is leucine or phenylalanine.

53. (New) The method of claim 49, wherein the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone has the following formula:



wherein each of R, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> is a hydrophobic substituent.

54. (New) The method of claim 53, wherein each of R, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> is independently selected from the group consisting of



55. (New) The method of claim 53, wherein R<sup>2</sup> and R<sup>3</sup> are and the compound is selected from the group consisting of

*Sub C1*

compound 1 (R<sup>1</sup>= and R= ),

compound 2 (R<sup>1</sup>= and R= ),

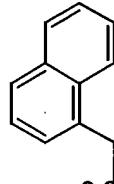
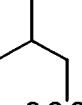
compound 3 (R<sup>1</sup>= and R= ),

compound 4 (R<sup>1</sup>= and R= ),

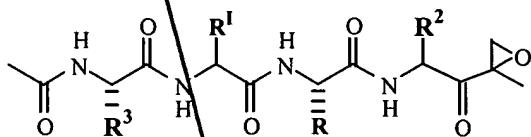
compound 5 (R<sup>1</sup>= and R= ),

compound 6 (R<sup>1</sup>= and R= ) and

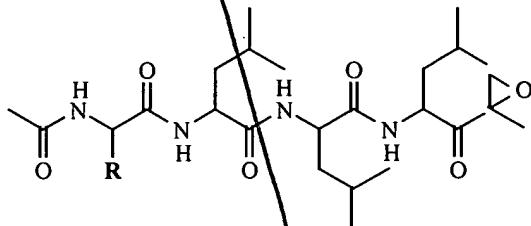
*13*  
cont

compound 7 ( $R^1 =$   and  $R =$  ).

56. (New) The method of claim 53, wherein the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone has the following stereo-configuration:

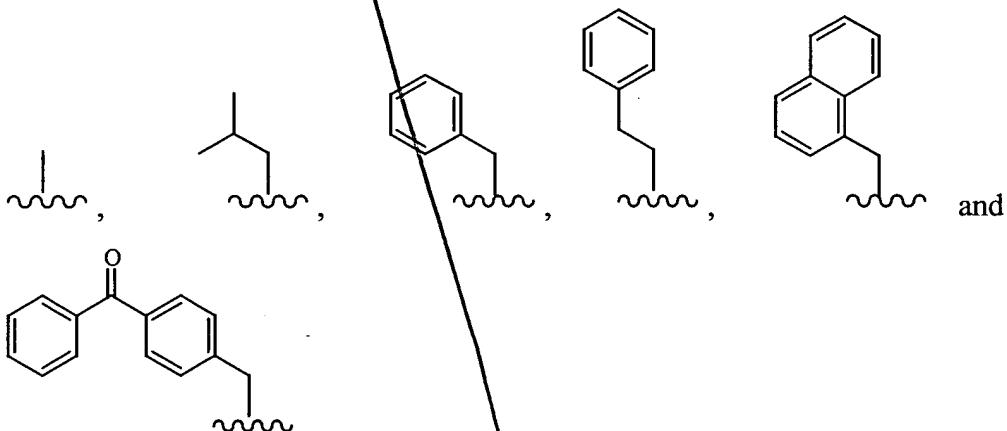


57. (New) The method of claim 49, wherein the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone has the following formula:

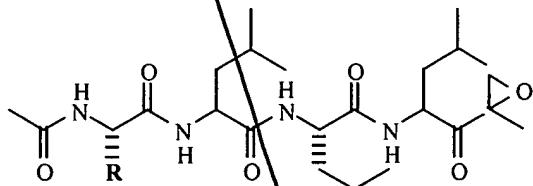


*bulk C1*

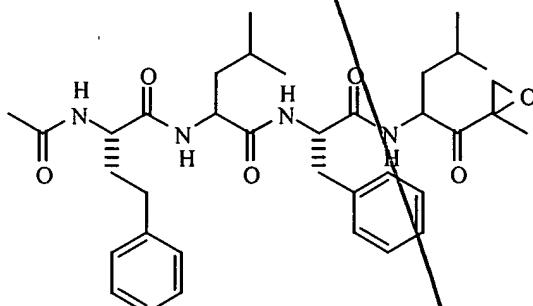
wherein R is selected from the group consisting of



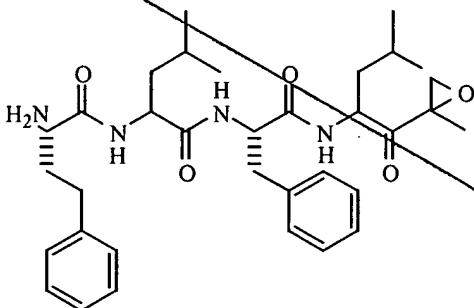
58. (New) The method of claim 57, wherein the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone has the following stereo-configuration:



59. (New) The method of claim 58, wherein the peptide  $\alpha'$ ,  $\beta'$ -epoxyketone is

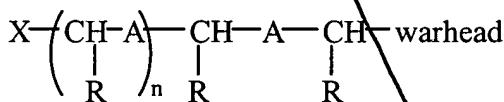


60. (New) The method of claim 45, wherein the compound is selected from the group consisting of



, PS-341, NLVS, PSI epoxide, lactacystin and PTX.

61. (New) The method of claim 45, wherein the compound has the following formula:



wherein the warhead reacts irreversibly with the catalytic chymotrypsin site of the proteasome;

A is independently CO-NH or isostereomer thereof;

R is independently a hydrocarbyl;

X is a polar group; and

n = 0-2.

62. (New) The method of claim 61, wherein R contains a substituted group selected from the group consisting of a halo group, -OR, -SR, -NR<sub>2</sub>, =O, -COR, -OCOR, -NHCOR, -NO<sub>2</sub>, -CN, and -CF<sub>3</sub>.

63. (New) The method of claim 61, wherein X is protected.

64. (New) The method of claim 25, wherein said subject is a human.

65. (New) The method of claim 25, wherein said condition to be treated is selected from the group consisting of male pattern baldness, alopecia caused by chemotherapy, hair thinning due to aging, and genetic disorders.

66. (New) The method of claim 1, wherein said subject is a non-human mammal.

67. (New) The method of claim 66, wherein said hair growth provides additional protection from cold temperatures.

68. (New) The method of claim 25, wherein said hair growth is due to thickened hair sheath diameter, increased hair diameter, differentiation of quiescent hair follicles into more mature forms, increased rate of growth in hair length and/or thickness, or the appearance of proliferation of new hair follicles.

69. (New) The method of claim 25, wherein said compound is co-administered with an agent promoting skin tissue growth or infiltration.

70. (New) The method of claim 69, wherein said agent is selected from the group consisting of an epidermal growth factor, a fibroblast growth factor, a platelet-derived growth